

## **EXHIBIT 15**



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Application No. 97 917 856.3 - 2403	Ref. B6539-CAGCO	Date 26.11.2007
Applicant PROGENICS PHARMACEUTICALS, INC.		

**Decision to refuse a European Patent application**

The Examining Division - at the oral proceedings dated 07.11.2007 - has decided:

**European Patent application No. 97 917 856.3 is refused.**

**Applicant/s:**  
PROGENICS PHARMACEUTICALS, INC.  
777 Old Saw Mill River Road  
Tarrytown, NY 10591  
US

**Title**  
METHOD FOR PREVENTING HIV-1 INFECTION OF CD4+  
CELLS

**The grounds for the decision are set out on the supplemental sheets annexed hereto.**

**Possibility of appeal**

This decision is open to appeal.  
Attention is drawn to the attached text of Articles 106 to 108 EPC.

Applicants: Graham P. Allaway et al.  
Serial No.: 09/888,938  
Filed: June 25, 2001  
**Exhibit 15**



Date 26.11.2007

Sheet 2

Application No.: 97 917 856.3

**Examining Division:**

<b>Chairman:</b>	Vollbach, Silke
<b>2nd Examiner:</b>	Mueller, Frank
<b>1st Examiner:</b>	Grötzinger, Thilo



PEPPER CANO, E  
**Formalities Officer**  
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Enclosure(s): 8 page/s reasons (Form 2916)  
Form 2019  
Main Request, Auxiliary Requests I to V

to EPO postal service: 21.11.07



## 1. SUMMARY OF FACTS AND SUBMISSIONS

- 1.1 European patent application EP 97 917 856.3 originated from the international patent application PCT/US97/05597 which was filed on 2 April 1997 and entered the regional phase in Europe on 2 November 1998.
- 1.2 With communications dated 9 May 2003, 27 January 2004, 5 August 2004, 1 April 2005, and 27 January 2006 the Applicant was informed that the application was regarded as lacking unity (Article 82 EPC), clarity (Article 84 EPC), novelty (Article 54), inventive step (Article 56 EPC), and disclosing the claimed subject-matter insufficiently (Article 83 EPC). Moreover, the amended claimed subject-matter was considered to extend beyond the content of the application as filed (Article 123(2) EPC).
- 1.3 On 6 July 2005 observations were filed by a third party pursuant to Article 115(1) EPC.
- 1.4 With letters of reply of 19 November 2003, 1 July 2004, 14 February 2005, 11 October 2005, and 7 August 2006 new claims sets were filed in order to overcome the objections.
- 1.5 On 5 May 2007 the Applicant (AP) was summoned to attend oral proceedings.
- 1.6 With letter of 5 October 2007, the AP filed final observations including a new Main Request (MR) and Auxiliary Requests I to III (ARs I to III).
- 1.7 Oral proceedings were duly held on 7 November 2007. During the oral proceedings a new MR and AR I were filed. The previous MR and ARs I to III became AR III, AR IV, AR V, and AR II, respectively (see also the Annex).

## 2. DECISION

At the end of the oral proceedings the Chairwoman announced the decision that the European patent application EP 97 917 856.3 is refused according to Article 97(1)



EPC because none of the requests meets the requirements of the EPC.

### 3. REASONS FOR THE DECISION

- 3.1 The claims of European patent application EP 97 917 856.3 relate to antibodies directed against a chemokine receptor and capable of inhibiting infection of human CD4<sup>+</sup> cells by HIV, and to the medical use thereof.

#### 3.2 Main Request (MR)

##### 3.2.1 Amendments (Article 123(2) EPC)

The Examining Division (ED) is of the opinion that claim 1 of the MR extends beyond the content of the application as filed. In particular, no basis can be found in the application for the feature "capable of binding to a human CCR5 chemokine receptor on the surface of a CD4<sup>+</sup> cell".

The AP cited various passages (claim 2 in combination with claim 5, page 36, lines 2 to 5, page 27, lines 25 to 30, page 12, lines 12 to 16, page 1, lines 17 to 21, and the title) and submitted that these passages together form a basis for the above-mentioned feature. In other words, this feature is not explicitly but implicitly disclosed in the application.

However, apart from the fact that certain of the cited passages cannot be used as a basis (e.g. page 1, lines 17 to 21, belongs to the background-section), the ED is of the opinion that a combination of all the passages is not allowable and, therefore, that the above feature is, even implicitly, not supported by the description. While the passages disclose CD4<sup>+</sup> cells, (unspecified) chemokine receptors on target cells, (unspecified) antibodies against (unspecified) chemokine receptors, and the fact that CCR5 can confer HIV-cell fusion, the application lacks any teaching that would allow the person skilled in the art to clearly and unambiguously conclude that these passages have to be read together. In any case, a selection of anti-CCR5 antibodies out of antibodies recognising any chemokine receptor is not clearly and unambiguously derivable from the application as filed.

Thus, while the feature "capable of binding to a human CCR5 chemokine receptor on the surface of a CD4<sup>+</sup> cell" might be regarded as being obvious in view of a



combination of the cited passages, these passages do not form an implicit disclosure of this feature. Claim 1 of the MR therefore violates the requirements of Article 123(2) EPC.

### 3.3 Auxiliary Request III (AR III)

#### 3.3.1 Amendments (Article 123(2) EPC)

Likewise, the Examining Division (ED) is of the opinion that claim 1 of the AR III extends beyond the content of the application as filed. In particular, a basis is missing in the application for the feature "expressed in a mammalian cell line".

During the written proceedings, the AP argued that support for claim 1 of the then MR can be found on page 22 of the present application, lines 16 to 18, in combination with lines 27 to 30. In particular, the opinion was expressed that according to page 22 antibody production is performed in parallel to the RET assay and follows directly the receptor expression step. Therefore, the phrase "following expression" can only be read on the expression of the receptors in mammalian cell lines.

This opinion cannot be followed. In particular, it does not appear to be scientifically prudent and logical, as stated by the AP, to immediately raise (monoclonal) antibodies against any expressed receptor before knowing whether or not the receptor is likely to be involved in HIV-cell fusion. The step of antibody production only follows after the RET assay and with receptors that have previously been identified in the RET assay and shown to confer fusion capability in order to save time and costs. Thus, from these passages it neither follows for the person skilled in the art that antibodies are produced directly after the receptor expression step nor that the phrase "following expression" refers to this step. The ED maintains that rather page 22 is silent about the system in which the antigens are expressed for the generation of antibodies.

In addition, it is noted that even if the reasoning of the AP was accepted, page 22 does not disclose the expression of receptors in (any) mammalian cell line but only in mammalian cell lines which express human CD4 but do not fuse with HeLa-env<sub>JR-FL</sub> or HeLa-env<sub>LA1</sub> (see page 22, lines 16 to 20). Thus, under no circumstances this passage can serve as a basis for the feature "expressed in a mammalian cell line". Claim 1 of AR III is thus regarded to be not allowable under Article 123(2) EPC.



3.3.2 During the oral proceedings, the Applicant neither wanted to further comment on AR III nor on the objections raised under Article 123(2) EPC.

### 3.4 Auxiliary Requests I and IV (ARs I and IV)

#### 3.4.1 Priority (Articles 87 to 89 EPC)

The ED is of the opinion that monoclonal antibodies prepared against an expressed human CCR5 chemokine receptor and capable of inhibiting HIV infection as claimed in claim 1 of AR I and AR IV are not directly and unambiguously derivable from the first priority document 08/627,684 of the present application and, consequently, that these claims do not enjoy 2 April 1996 as the effective filing date.

The AP essentially argued that particularly the "first series of experiments" was present in the first priority document and that the procedure described under point 3 of the experiments "Cloning the chemokine receptors" inevitably leads to the CCR5 chemokine receptor. Consequently, antibodies as claimed in claim 1 of AR I and AR IV are implicitly disclosed in the first priority document and, following the principles laid down in G2/98, enjoy the first priority date.

However, it is noted that claim 1 of AR I and AR IV relates to monoclonal antibodies directed against CCR5 and further being functionally characterised in that they can inhibit HIV infection of CD4<sup>+</sup> cells. That an antibody with these features can indeed be prepared is not even disclosed in the present application, let alone in the first priority document. The first priority document only discloses that certain chemokines can inhibit the fusion of certain strains of HIV (see, e.g., page 2, line 32, to page 3, line 2) and thus extends the teaching of Cocchi et al. (D1) in that the inhibition takes place at the fusion step. On page 22 of the first priority document, a method for identifying and cloning chemokine receptors that are required for HIV-1 fusion is disclosed followed by a method for screening for antibodies with a certain desired property. The ED cannot see how from these methods a person skilled in the art can directly and unambiguously derive the product of claim 1 of AR I and AR IV, namely a monoclonal antibody prepared against an expressed human CCR5 chemokine receptor and capable of inhibiting HIV infection.

For the above reasons, claim 1 of AR I and AR IV does not enjoy the first priority date (Articles 87 to 89 EPC).



### 3.4.2 Novelty (Article 54 EPC)

Claim 1 of AR I and AR IV lacks novelty pursuant to Article 54 EPC over, e.g., WO97/45543 (D4).

This PCT application was published on 4 December 1997 and claims the priority date of 28 May 1996, which is earlier than 14 June 1996, the second priority date of the present application. It has been supplied to the European Patent Office in one of its official languages and the national fee provided for in Article 22, paragraph 1 or Article 39, paragraph 1 of the Co-operation Treaty has been paid. The requirements of Article 158(2) EPC are thus fulfilled. Its content as filed is therefore considered as comprised in the state of the art relevant to the question of novelty, pursuant to Article 54(3) and (4) EPC.

With respect to the disclosure content of WO97/45543 (D4), the AP put forward that the antibodies disclosed in example 4 on page 52 of that document are raised against peptides derived from CCR5. Thus, these antibodies are different from the antibodies of the present application which are raised against an expressed CCR5 receptor, i.e. a receptor which is functional and inserted into the cell membrane. According to the AP, the term "expressed" is a distinctive feature and the term "receptor" a functional limitation such that the claimed antibodies can be seen as a formally new subpopulation of the antibodies disclosed in WO97/45543 (D4). Finally, Olson et al. (D5) was cited, a document disclosing monoclonal antibodies that recognise complex conformational epitopes on CCR5 (page 4151, left-hand column, lines 2 to 4) but not denatured CCR5 protein on Western blots (page 4147, right-hand column, lines 2 to 5).

The AP's reasoning is not deemed to be convincing. WO97/45543 (D4) discloses anti-CCR5 antibodies not only in example 4 on page 52 but also on page 21, first to third paragraph. Both passages are also present in the priority document of WO97/45543 (D4) on page 10, line 29, to page 11, line 11, and example 4 on page 43, and the contents are essentially identical. In particular on page 21 of WO97/45543 (D4) monoclonal antibodies are disclosed (lines 22 to 24) that bind CCR5 and block *env*-mediated membrane fusion (lines 2 to 5). An example of such an antibody (prepared against an 28 amino acid N-terminal portion of CCR5) is shown to work in example 4. In other words, WO97/45543 (D4) discloses antibodies which are directed against





the same antigen and which inhibit HIV-1 infection.

The features "expressed" and "receptor" characterise, if at all, the antigen but not *prima facie* the antibody, and could be regarded as being distinctive only if they conferred to the claimed antibodies specific technical features. However, the ED is not aware of such features and therefore, the antibodies of the present application cannot be delimited from the antibodies of WO97/45543 (D4).

Regarding Olson et al. (D5), it is noted that this document is post-published. Moreover, it only reports on certain features of specifically disclosed monoclonal antibodies. This disclosure neither implies that only antibodies against conformational epitopes are inhibitory nor can it cast doubt as to the effect of the antibodies of WO97/45543 (D4). The latter is particularly true because, as mentioned above, WO97/45543 (D4) indeed discloses antibodies that are inhibitory.

Thus, WO97/45543 (D4) is prejudicial to the novelty of the subject-matter of claim 1 of AR I and AR IV insofar as the same contracting states are designated.

- 3.4.3 During the oral proceedings, the Applicant neither wanted to further comment on AR IV nor on the objections raised under Article 54 EPC.

### 3.5 Auxiliary Requests II and V (ARs II and V)

#### 3.5.1 Clarity (Article 84 EPC)

Claim 1 of AR II and AR V lacks clarity pursuant to Article 84 EPC.

The AP argued that in claim 1 of AR II and AR V the ligand binding profile "RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ " clearly indicates that the receptor can only be a C-C chemokine receptor. At the priority date only a small group of such chemokine receptors was known (CCR1 to CCR5), of which, furthermore, only CCR1, CCR3, and CCR5 would have been considered by the person skilled in the art to be of potential relevance due to the ligand binding profile. The AP continued that in fact only CCR5 is encompassed by the profile and that, therefore, not an indefinite number of antibodies is characterised by the mentioned ligand binding profile. Moreover, the application provides on page 17, line 33, to page 18, line 15, an assay (RET-assay) which allows for the testing of the functional feature "capable of inhibiting infection of a human CD4<sup>+</sup> cell by a HIV-1 virus". Hence, the scope of the claim is clear and supported by



the description.

The ED cannot agree to this opinion. It is firstly noted that at the first priority date of the present application the chemokine profiles of the various chemokine receptors were apparently not unequivocally resolved (compare page 30 of the present application, line 34, to page 31, line 2, and Samson et al. (D9), page 3362, second half of the right-hand column, disclosing divergent profiles for the chemokine receptor CCR1). It is thus questionable whether chemokine binding profiles were at all appropriate to clearly and unambiguously define certain chemokine receptors at the date of filing of the first priority document.

Even if this aspect was disregarded, the ED is of the opinion that the profile reads "RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ " (emphasis added) and not "RANTES, MIP-1 $\alpha$  and MIP-1 $\beta$ ". The profile of claim 1 is unclear, in particular in combination with the functional feature present in the claim. Due to the "or"-combination of the three chemokines and based on the information provided by the AP during the oral proceedings, this profile appears to read only on the CCR3 receptor, which is the only chemokine receptor that binds only one of the mentioned chemokines, namely RANTES. However, this receptor cannot, according to the submissions of the AP and the disclosure, e.g., on page 35 of the present application, lines 31 to 34, permit HIV-cell fusion.

Thus, claim 1 is unclear according to Article 84 EPC because of an inconsistency between the claim and the description.

The ED is furthermore convinced that claim 1 would remain unclear even if the profile was interpreted in the "and/or"-sense. In this case the profile would clearly encompass several chemokine receptors in addition to CCR5 and consequently, this feature would again be inconsistent with the description that shows that only CCR5 mediates fusion. For this reason alone, the claim cannot be allowed under Article 84 EPC.

Moreover, in view of the ED, the functional feature "capable of inhibiting infection of a human CD4<sup>+</sup> cell by a HIV-1 virus" cannot be used to remedy the inconsistency in the claim because an inconsistent, unclear definition is not rendered clear by a functional limitation.

In summary, the ligand binding profile "RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ " introduces an unclarity into claim 1 of AR II and AR V which is unacceptable under Article 84 EPC.

- 3.5.2 During the oral proceedings, the Applicant neither wanted to further comment on AR V nor on the objections raised under Article 84 EPC.

**Entscheidungsgründe (Anlage)****Grounds for the decision (Annex)****Motifs de la décision (Annexe)**

Datum  
Date 26.11.2007  
Date

Blatt  
Sheet 8  
Feuille

Anmelde-Nr.:  
Application No.: 97 917 856.3  
Demande n°:

**Article 106**  
**Decisions subject to appeal**

- (1) An appeal shall lie from decisions of the Receiving Section, Examining Divisions, Opposition Divisions and the Legal Division. It shall have suspensive effect.
- (2) An appeal may be filed against the decisions of the Opposition Division even if the European patent has been surrendered or has lapsed for all the designated States.
- (3) A decision which does not terminate proceedings as regards one of the parties can only be appealed together with the final decision, unless the decision allows separate appeal
- (4) The apportionment of costs of opposition proceedings cannot be the sole subject of an appeal.
- (5) A decision fixing the amount of costs of opposition proceedings cannot be appealed unless the amount is in excess of that laid down in the Rules relating to Fees.

**Article 107**  
**Persons entitled to appeal and to be parties to appeal proceedings**

Any party to proceedings adversely affected by a decision may appeal. Any other parties to the proceedings shall be parties to the appeal proceedings as of right.

**Article 108**  
**Time limit and form of appeal**

Notice of appeal must be filed in writing at the European Patent Office within **two months** after the date of notification of the decision appealed from. The notice shall not be deemed to have been filed until after the fee for appeal has been paid. Within **four months** after the date of notification of the decision, a written statement setting out the grounds of appeal must be filed.

**Further information concerning the filing of an appeal**

- (a) The appeal is to be filed with the European Patent Office either at its seat in Munich, at its branch at The Hague or at its Berlin sub-office. The postal addresses are as follows:

(i) European Patent Office D-80298 Munich Germany (Telex: 523656 epmu d) (Fax: +49 89 2399-4465)	(ii) European Patent Office Branch at The Hague Patentlaan 2 Postbus 5818 NL-2280 HV Rijswijk (ZH) Netherlands (Telex: 31651 epo nl) (Fax: +31 70 340-3016)	(iii) European Patent Office Berlin sub-office D-10958 Berlin Germany (Fax: +49 30 25901-840)
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- (b) The notice of appeal must contain the name and address of the appellant in accordance with the provisions of Rule 26(2)(c) EPC, and a **statement** identifying the decision which is impugned and the extent to which amendment or cancellation of the decision is requested (see Rule 64 EPC). The notice of appeal and any subsequent submissions stating the grounds for appeal must be signed.
- (c) Notice of appeal must be **filed in writing** (typewritten or printed (Rule 36(2) EPC), by telegram, telex or fax (Rule 36(5) EPC; OJ EPO 6/89, 219-225; OJ EPO 9/89, 396)).
- (d) The fee for appeal is laid down in the Rules relating to Fees. The equivalents in the national currencies in which the fee for appeal can be paid are regularly published in the Official Journal of the European Patent Office under the heading "Guidance for the payment of fees, costs and prices".

Application No.:

97 917 856.3

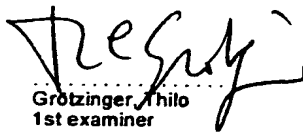
**Decision of the Examining Division**


In the oral proceedings held on 07.11.2007, the examining division has decided:

**The European patent application is refused on the basis of Art. 97 (1) EPC. The reasons for the decision are attached (Form(s) 2916).**

19-11-07  
Date

  
Vollbach, Silke  
Chairman

  
Grötzing, Thilo  
1st examiner

  
Mueller, Frank  
2nd examiner

Enclosure(s):      Form 2916  
Main Request, Auxiliary Requests I to V

## MAIN REQUEST

1. A monoclonal antibody, or a portion thereof, <sup>Capable of binding to</sup> ~~prepared~~ <sup>on the surface of a CD4<sup>+</sup> cell</sup> ~~against~~ a human CCR5 chemokine receptor ~~expressed in a mammalian cell line, which receptor binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , and wherein the antibody is capable of~~ inhibiting infection of a human CD4<sup>+</sup> cell by a HIV-1 virus.
2. A monoclonal antibody or a portion thereof according to claim 1 which is capable of inhibiting fusion of the HIV-1 to CD4<sup>+</sup> cells, and the HIV-1 is macrophagetropic.
3. The monoclonal antibody of claim 1 or 2.
4. The monoclonal antibody portion of claim 1 or 2.
5. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
6. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
7. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

8. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
9. A pharmaceutical composition comprising the monoclonal antibody of claim 3 and a pharmaceutically acceptable carrier.
10. The pharmaceutical composition of claim 9, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.
11. A pharmaceutical composition comprising the monoclonal antibody portion of claim 4 and a pharmaceutically acceptable carrier.
12. The pharmaceutical composition of claim 11, wherein the monoclonal antibody portion is present in an amount effective to inhibit HIV-1 infection.
13. A composition of matter comprising a monoclonal antibody of claim 3 linked to a compound capable of increasing the *in vivo* half-life of the antibody.
14. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
15. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

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16. A composition of matter comprising a monoclonal antibody portion of claim 4 linked to a compound capable of increasing the *in vivo* half-life of the monoclonal antibody portion.
17. Use of the composition of matter of claim 16 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
18. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
19. The composition of matter of claim 13 or 14, wherein the compound is polyethylene glycol.
20. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
21. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
22. A pharmaceutical composition comprising the composition of matter of any one of claims 13, 16 or 19 and a pharmaceutically acceptable carrier.

CA



23. The pharmaceutical composition of claim 22, wherein the amount of the composition of matter is effective to inhibit HIV-1 infection.
24. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.
25. The antibody according to claim 24 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.
26. The antibody according to claim 24 or 25 which is monoclonal.
27. A pharmaceutical composition comprising an amount of the antibody of claim 24 or 25 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.
28. The antibody according to claim 24 or 25 for use in HIV-1 therapy.
29. Use of an antibody according to claim 24 or 25 for the manufacture of a medicament for inhibiting HIV-1 infection.
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## AUXILIARY REQUEST I

1. A monoclonal antibody, or a portion thereof, prepared against an expressed human CCR5 chemokine receptor, ~~/which receptor binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ /~~ and wherein the antibody is capable of inhibiting infection of a human CD4<sup>+</sup> cell by a HIV-1 virus.
2. A monoclonal antibody or a portion thereof according to claim 1 which is capable of inhibiting fusion of the HIV-1 to CD4<sup>+</sup> cells, and the HIV-1 is macrophagetropic.
3. The monoclonal antibody of claim 1 or 2.
4. The monoclonal antibody portion of claim 1 or 2.
5. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
6. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
7. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
8. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

GA

9. A pharmaceutical composition comprising the monoclonal antibody of claim 3 and a pharmaceutically acceptable carrier.
10. The pharmaceutical composition of claim 9, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.
11. A pharmaceutical composition comprising the monoclonal antibody portion of claim 4 and a pharmaceutically acceptable carrier.
12. The pharmaceutical composition of claim 11, wherein the monoclonal antibody portion is present in an amount effective to inhibit HIV-1 infection.
13. A composition of matter comprising a monoclonal antibody of claim 3 linked to a compound capable of increasing the *in vivo* half-life of the antibody.
14. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
15. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
16. A composition of matter comprising a monoclonal antibody portion of claim 4 linked to a compound

capable of increasing the *in vivo* half-life of the monoclonal antibody portion.

17. Use of the composition of matter of claim 16 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
18. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
19. The composition of matter of claim 13 or 14, wherein the compound is polyethylene glycol.
20. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
21. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
22. A pharmaceutical composition comprising the composition of matter of any one of claims 13, 16 or 19 and a pharmaceutically acceptable carrier.
23. The pharmaceutical composition of claim 22, wherein the amount of the composition of matter is effective to inhibit HIV-1 infection.

24. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.
25. The antibody according to claim 24 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.
26. The antibody according to claim 24 or 25 which is monoclonal.
27. A pharmaceutical composition comprising an amount of the antibody of claim 24 or 25 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.
28. The antibody according to claim 24 or 25 for use in HIV-1 therapy.
29. Use of an antibody according to claim 24 or 25 for the manufacture of a medicament for inhibiting HIV-1 infection.
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II  
AUXILIARY REQUEST ~~III~~

1. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.
  2. The antibody according to claim 1 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.
  - 3.. The antibody according to claim 1 or 2 which is monoclonal.
  4. A pharmaceutical composition comprising an amount of the antibody of claim 1 or 2 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.
  5. The antibody according to claim 1 or 2 for use in HIV-1 therapy.
  6. Use of an antibody according to claim 1 or 2 for the manufacture of a medicament for inhibiting HIV-1 infection.
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AUXILIARY REQUEST III  
~~MAIN REQUEST~~

1. A monoclonal antibody, or a portion thereof, prepared against a human CCR5 chemokine receptor expressed in a mammalian cell line, which receptor binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , and wherein the antibody is capable of inhibiting infection of a human CD4<sup>+</sup> cell by a HIV-1 virus.
2. A monoclonal antibody or a portion thereof according to claim 1 which is capable of inhibiting fusion of the HIV-1 to CD4<sup>+</sup> cells, and the HIV-1 is macrophagetropic.
3. The monoclonal antibody of claim 1 or 2.
4. The monoclonal antibody portion of claim 1 or 2.
5. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
6. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
7. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

8. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
9. A pharmaceutical composition comprising the monoclonal antibody of claim 3 and a pharmaceutically acceptable carrier.
10. The pharmaceutical composition of claim 9, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.
11. A pharmaceutical composition comprising the monoclonal antibody portion of claim 4 and a pharmaceutically acceptable carrier.
12. The pharmaceutical composition of claim 11, wherein the monoclonal antibody portion is present in an amount effective to inhibit HIV-1 infection.
13. A composition of matter comprising a monoclonal antibody of claim 3 linked to a compound capable of increasing the *in vivo* half-life of the antibody.
14. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
15. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.



16. A composition of matter comprising a monoclonal antibody portion of claim 4 linked to a compound capable of increasing the *in vivo* half-life of the monoclonal antibody portion.
17. Use of the composition of matter of claim 16 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
18. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
19. The composition of matter of claim 13 or 14, wherein the compound is polyethylene glycol.
20. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
21. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
22. A pharmaceutical composition comprising the composition of matter of any one of claims 13, 16 or 19 and a pharmaceutically acceptable carrier.

23. The pharmaceutical composition of claim 22, wherein the amount of the composition of matter is effective to inhibit HIV-1 infection.
24. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.
25. The antibody according to claim 24 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.
26. The antibody according to claim 24 or 25 which is monoclonal.
27. A pharmaceutical composition comprising an amount of the antibody of claim 24 or 25 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.
28. The antibody according to claim 24 or 25 for use in HIV-1 therapy.
29. Use of an antibody according to claim 24 or 25 for the manufacture of a medicament for inhibiting HIV-1 infection.
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IV  
AUXILIARY REQUEST *X*

1. A monoclonal antibody, or a portion thereof, prepared against an expressed human CCR5 chemokine receptor, which receptor binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , and wherein the antibody is capable of inhibiting infection of a human CD4<sup>+</sup> cell by a HIV-1 virus.
2. A monoclonal antibody or a portion thereof according to claim 1 which is capable of inhibiting fusion of the HIV-1 to CD4<sup>+</sup> cells, and the HIV-1 is macrophagetropic.
3. The monoclonal antibody of claim 1 or 2.
4. The monoclonal antibody portion of claim 1 or 2.
5. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
6. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
7. Use of the monoclonal antibody of claim 3 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
8. Use of the monoclonal antibody portion of claim 4 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection. *GX*

9. A pharmaceutical composition comprising the monoclonal antibody of claim 3 and a pharmaceutically acceptable carrier.
10. The pharmaceutical composition of claim 9, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.
11. A pharmaceutical composition comprising the monoclonal antibody portion of claim 4 and a pharmaceutically acceptable carrier.
12. The pharmaceutical composition of claim 11, wherein the monoclonal antibody portion is present in an amount effective to inhibit HIV-1 infection.
13. A composition of matter comprising a monoclonal antibody of claim 3 linked to a compound capable of increasing the *in vivo* half-life of the antibody.
14. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
15. Use of the composition of matter of claim 13 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
16. A composition of matter comprising a monoclonal antibody portion of claim 4 linked to a compound

capable of increasing the *in vivo* half-life of the monoclonal antibody portion.

17. Use of the composition of matter of claim 16 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
18. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
19. The composition of matter of claim 13 or 14, wherein the compound is polyethylene glycol.
20. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.
21. Use of the composition of matter of claim 19 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.
22. A pharmaceutical composition comprising the composition of matter of any one of claims 13, 16 or 19 and a pharmaceutically acceptable carrier.
23. The pharmaceutical composition of claim 22, wherein the amount of the composition of matter is effective to inhibit HIV-1 infection.

24. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.
25. The antibody according to claim 24 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.
26. The antibody according to claim 24 or 25 which is monoclonal.
27. A pharmaceutical composition comprising an amount of the antibody of claim 24 or 25 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.
28. The antibody according to claim 24 or 25 for use in HIV-1 therapy.
29. Use of an antibody according to claim 24 or 25 for the manufacture of a medicament for inhibiting HIV-1 infection.
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V  
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AUXILIARY REQUEST *11*

1. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1 $\alpha$  or MIP-1 $\beta$ , which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.
2. The antibody according to claim 1 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.
3. The antibody according to claim 1 or 2 which is monoclonal.
4. The antibody according to claim 1 which is prepared against the CCR5 receptor.
5. A pharmaceutical composition comprising an amount of the antibody of claim 1 or 2 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.
6. The antibody according to claim 1 or 2 for use in HIV-1 therapy.
7. Use of an antibody according to claim 1 or 2 for the manufacture of a medicament for inhibiting HIV-1 infection.